Supplementary Online Content

Thompson AM, Hu T, Eshelbrenner CL, Reynolds K, He J, Bazzano LA. Antihypertensive treatment and secondary prevention of cardiovascular disease events among persons without hypertension: a meta-analysis. *JAMA*. 2011;305(9):913-922.

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Definitions of Outcomes for Each Randomized Controlled Trial Included in the Meta-analysis

Trial	Fatal or Nonfatal Stroke	Fatal or Nonfatal MI	Fatal or Nonfatal CHF	Fatal or Nonfatal Composite Outcome	CVD Mortality	All-cause mortality
MIS,[22] 1975					Cardiovascular deaths	
MPI,[23] 1980						Total mortality
BHAT,[24] 1982						Total mortality
ASPS,[25] 1983						Total mortality
CONSENSUS II,[26,27] 1992						Total mortality
SOLVD,[28-31] 1995	Fatal or nonfatal stroke	Fatal or nonfatal acute MI	Hospitalization for CHF	MI, unstable angina, CVD mortality		Total mortality
USCHF,[32] 1996						Total mortality
TRACE,[33,34] 1997		Fatal or nonfatal recurrent MI	Hospitalization or death due to severe CHF		Cardiovascular death	Total mortality
AIRE,[35,36] 1999			Severe/resistant CHF (clinical judgment, usually grade IV, and unresponsive to non-ACEI treatment		Cardiovascular death	Total mortality
SMILE,[37-39] 1999		Fatal or nonfatal recurrent MI	Mild-to-moderate CHF (NYHA classification I-IV)	All-cause mortality or severe CHF		6 week mortality
MERIT-HF,[40] 2000			Total mortality or hospitalization for worsening CHF	All-cause mortality/hospitalization		
CCS-1,[41,42] 2001						Total mortality
HOPE,[43-46] 2001				CVD death, MI, or stroke		
ABCD,[14,47] 2002	Nonfatal stroke	Nonfatal MI	Hospitalization for CHF		Death due to CVD event: sudden death, progressive CHF, fatal MI, fatal arrhythmias, stroke, ruptured aortic aneurysm	Total mortality

eTable 1 (Continued)

Trial	Fatal or Nonfatal Stroke	Fatal or Nonfatal MI	Fatal or Nonfatal CHF	Fatal or Nonfatal Composite Outcome	CVD Mortality	All-cause mortality
CAMELOT,[12] 2004				Adverse CVD events: CVD death, nonfatal MI, resuscitated cardiac arrest, coronary revascularization, hospitalization for angina pectoris, hospitalization for CHF, fatal or nonfatal stroke, TIA, new diagnosis of PVD.		
COPERNICUS,[48,49] 2004			Death or Hospitalization for CHF	All-cause mortality or CVD hospitalization		Total mortality
DIABHYCAR,[50] 2004				Combined incidence of CVD death (including sudden death), non-fatal acute MI, stroke, CHF requiring admission to hospital, end stage renal failure		
PEACE,[51-53] 2004	Nonfatal stroke	Nonfatal MI		Death from CVD causes or nonfatal MI, or coronary revascularization	Cardiovascular death	Total mortality
SAVE,[54,55] 2004	Nonfatal or fatal stroke	Nonfatal or fatal recurrent MI	Overt CHF requiring hospitalization or persisting despite administration of diuretic agents and digitalis necessitating open label therapy with ACEI	Combined CVD events: death from CVD causes, CHF, recurrent MI, or stroke	Cardiovascular death	Total mortality
PROGRESS,[56-58] 2006	Nonfatal or fatal stroke					Total mortality
ADVANCE,[59,60] 2007				Major macrovascular events (CVD, nonfatal MI, nonfatal stroke) and major microvascular events (new or worsening nephropathy or retinopathy)		
PRoFESS,[61,62] 2008	Nonfatal or fatal recurrent stroke			CVD death, MI, recurrent stroke, or worsening or new CHF		
TRANSCEND,[15] 2008				CVD death, MI, recurrent stroke, or worsening or new CHF		
EUROPA,[13],[63,64] 2009				CVD death, nonfatal MI, cardiac arrest with successful resuscitation		
PATS,[65] 2009	Nonfatal or fatal stroke					

Abbreviations: MI, myocardial infarction; CHF, congestive heart failure; CVD, cardiovascular disease; ACEI, angiotensin-converting enzyme inhibitor; TIA, transient ischemic attack; PVD, peripheral vascular disease; CAD, Coronary artery disease; AF, atrial fibrillation.

eTable 2. Study-Specific Definitions Used to Identify Persons Without Hypertension Who Were Included in the Data Analysis

Trial	Definition of Participants without Hypertension
MIS,[22] 1975	Baseline DBP ≤ 78 mm Hg
MPI,[23] 1980	Baseline DBP below mean (<79.7 mm Hg in placebo group, < 79.2 mm Hg in treatment group)
BHAT,[24] 1982	Baseline DBP ≤ 76 mm Hg
ASPS,[25] 1983	No history of hypertension
CONSENSUS II,[26,27] 1992	No history of hypertension
SOLVD,[28-31] 1995	No history of hypertension
USCHF,[32] 1996	SBP below median (<115 mm Hg)
TRACE,[33,34] 1997	No history of hypertension (clinical diagnosis having resulted in medical therapy)
AIRE,[35,36] 1999	No history of hypertension (clinical diagnosis for which medical therapy was still being taken); treatment with antihypertensive medications was for reason other than hypertension.
SMILE,[37-39] 1999	No history of hypertension (clinical diagnosis having resulted in medical therapy)
MERIT-HF,[40] 2000	No history of hypertension
CCS-1,[41,42] 2001	SBP<140 mm Hg before study entry
HOPE,[43-46] 2001	Below median baseline SBP (<138 mm Hg)
ABCD,[14,47] 2002	Baseline DBP 80-89 mm Hg and not receiving antihypertensive medications[a]
CAMELOT,[12] 2004	Mean sitting SBP at baseline ≤ mean (129.5 and 128.9 mm Hg in treatment and placebo groups)
COPERNICUS,[48,49] 2004	SBP ≤ 125 mm Hg[b]
DIABHYCAR,[50] 2004	Baseline BP ≤ 140/90 mm Hg and not taking antihypertensive drugs.
PEACE,[51-53] 2004	Baseline BP < 140/90 mm Hg
SAVE,[54,55] 2004	No history of hypertension (clinical diagnosis having resulted in medical therapy or SBP≥140 mm Hg or DBP ≥90 mm Hg)
PROGRESS,[56-58] 2006	Baseline SBP<140 mm Hg
ADVANCE,[59,60] 2007	No history of hypertension (defined as treatment with antihypertensive medications, SBP > 140 mm Hg, DBP > 90 mm Hg at study entry)
PRoFESS,[61,62] 2008	Baseline SBP ≤ 135 mm Hg
TRANSCEND,[15] 2008	Baseline SBP ≤ 133 mm Hg[c]
EUROPA,[13],[63,64] 2009	Baseline SBP <140 mm Hg[d]
PATS,[65] 2009	Baseline BP < 140/90 mmHg

SBP = systolic blood pressure; DBP = diastolic blood pressure; RR=risk ratio; CI = confidence interval.

[a]The "moderate therapy group" was given placebo and considered as the placebo group for the purpose of this meta-analysis; "intensive therapy group" received either nisoldipine or enalapril as the primary antihypertensive medication and was considered as the treatment group. A total of 26 subjects with DBP 80-89 mm Hg and SBP >160 mm Hg were enrolled in the study in the first year.

[b]The RR (95% CI) were calculated from pooled estimates of effect in Figure 2.[48]

[c]The RR (95% CI) was estimated from Figure 4.[15]

[d]The RR (95% CI) was calculated from pooled estimates of effect in Figure 2a.[13]

eTable 3. Sensitivity Analyses According to Outcome

Outcome	No. of Studies	Pooled RR (95% CI)	Heterogeneity		
			I^2 (%)	χ^2	p-value
Composite outcome					
Overall	**13**	**0.85 (0.80, 0.90)**	**35.4**	**18.6**	**0.10**
Baseline use of β-blockers or diuretics < 50%	8	0.84 (0.77, 0.91)	44.8	12.67	0.08
History of HTN in definition of normotensive	6	0.86 (0.79, 0.94)	42.3	8.65	0.12
Sample size < median (n=1939)	4	0.77 (0.67, 0.87)	31.3	4.36	0.225
Study duration < median (25.1 months)	4	0.81 (0.72, 0.93)	47.6	5.73	0.13
Study year ≥ median (2001)	10	0.85 (0.79, 0.92)	42.3	15.6	0.08
All Cause Mortality					
Overall	**15**	**0.87 (0.80, 0.95)**	**46.1**	**25.98**	**0.03**
Baseline use of β-blockers or diuretics < 50%	12	0.88 (0.81, 0.95)	39.3	18.14	0.08
History of HTN in definition of normotensive	8	0.89 (0.83, 0.96)	8.3	7.63	0.37
Sample size < median (n=1939)	9	0.82 (0.71, 0.95)	44.7	14.46	0.07
Study duration < median (25.1 months)	8	0.86 (0.72, 1.03)	67.3	21.44	0.003
Study year ≥ median (2001)	6	0.88 (0.79, 0.98)	20.8	6.32	0.28

eTable 4. Subgroup Analyses of Comorbid Conditions and Antihypertensive Treatment According to Outcome

Outcome	Subgroup	No. of Studies	Pooled RR (95% CI)	Heterogeneity		
				I^2 (%)	χ^2	p-value
Composite CVD Outcome	**Overall**	**13**	**0.85 (0.80, 0.90)**	**35.4**	**18.56**	**0.10**
	Participants with History of MI or CAD:					
	All	5	0.83(0.75, 0.93	47.8	7.66	0.11
	Some	6	0.87 (0.81, 0.94)	22.1	6.42	0.27
	None	2	0.80 (0.63, 1.01)	75.1	4.01	0.05
	Participants with History of CHF					
	All	3	0.78 (0.68, 0.91)	60.0	5.00	0.08
	Some	0	--	--	--	--
	None	8	0.86 (0.79, 0.93)	34.6	10.70	0.15
	No information	2	0.90 (0.82, 0.99)	0.0	0.05	0.82
	Participants with History of Diabetes					
	All	2	0.95 (0.84, 1.08)	0.0	0.99	0.32
	Some	10	0.85 (0.81, 0.90)	18.4	11.03	0.27
	No Information	1	0.70 (0.57, 0.86)	--	--	--
	Antihypertensive Treatment					
	ACE Inhibitor	7	0.85 (0.78, 0.93)	48.6	11.66	0.07
	Other	6	0.85 (0.79, 0.92)	27.5	6.90	0.23
All-Cause Mortality						
	Overall	**15**	**0.87 (0.80, 0.95)**	**46.1**	**25.98**	**0.03**
	Participants with History of MI or CAD:					
	All	9	0.89 (0.81, 0.99)	38.2	12.94	0.11
	Some	4	0.87 (0.71, 1.06)	66.2	8.87	0.03
	None	2	0.70 (0.52, 0.95)	8.3	1.09	0.30
	Participants with History of CHF:					
	All	4	0.72 (0.60, 0.91)	68.8	9.60	0.02
	Some	6	0.93 (0.80, 1.08)	49.2	9.85	0.08
	None	3	0.87 (0.77, 0.98)	0.0	0.47	0.79
	No information	2	1.08 (0.84, 1.36)	0.0	0.0	0.95
	Participants with a History of Diabetes					
	All	1	0.92 (0.50, 1.70)	--	--	--
	Some	12	0.90 (0.84, 0.96)	25.6	14.78	0.19
	No Information	2	0.51 (0.28, 0.92)	61.0	2.57	0.11
	Antihypertensive Treatment					
	ACE Inhibitor	8	0.89 (0.84, 0.95)	1.0	7.07	0.42
	Other	7	0.83 (0.63, 1.09)	66.1	17.68	0.01